

In the claims:

Please amend the claims as follows:

Claims 1-8. (Cancelled)

9. **(Currently amended)** An isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a K_d of $1 \times 10^{-10} M$ or less and a k_{off} rate constant of $1 \times 10^{-3} s^{-1}$ $0.1s^+$ or less, as determined by surface plasmon resonance, or which inhibits phytohemagglutinin blast proliferation in an *in vitro* phytohemagglutinin blast proliferation assay (PHA assay) with an IC_{50} of $1 \times 10^{-6} M$ or less.

10. **(Currently amended)** The isolated human antibody of claim 9, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-4} s^{-1}$ $1 \times 10^{-2}s^+$ or less, as determined by surface plasmon resonance, or which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of $1 \times 10^{-7} M$ or less.

11. **(Currently amended)** The isolated human antibody of claim 9, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-5} s^{-1}$ $+ \times 10^{-3}s^+$ or less, as determined by surface plasmon resonance, or which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of $1 \times 10^{-8} M$ or less.

142. **(New)** The isolated human antibody, or antigen-binding portion thereof, of claim 9, which is a recombinant antibody, or antigen-binding portion thereof.

143. **(New)** The isolated human antibody of any one of claims 9 to 11, wherein the antibody is a neutralizing antibody.

144. **(New)** The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of $1 \times 10^{-7} M$ or less.

145. (New) The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC₅₀ of 1 x 10⁻⁸ M or less

12. (Currently amended) The isolated human neutralizing antibody of claim 143 9, or an antigen-binding portion thereof, ~~which dissociates from human IL-12 with a k_{off} rate constant of 1 x 10⁻⁴s⁻¹ or less, as determined by surface plasmon resonance, or~~ which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC₅₀ of 1 x 10⁻⁹ M or less.

13. (Currently amended) The isolated human neutralizing antibody of claim 143 9, or an antigen-binding portion thereof, ~~which dissociates from human IL-12 with a k_{off} rate constant of 1 x 10⁻⁵s⁻¹ or less, as determined by surface plasmon resonance, or~~ which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC₅₀ of 1 x 10⁻¹⁰M or less.

14. (Currently amended) The isolated human neutralizing antibody of claim 143 9, or an antigen-binding portion thereof, ~~which dissociates from human IL-12 with a k_{off} rate constant of 1 x 10⁻⁵s⁻¹ or less, as determined by surface plasmon resonance, or~~ which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC₅₀ of 1 x 10⁻¹¹M or less.

146. (New) The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC₅₀ of 1 x 10⁻¹⁰ M or less.

147. (New) The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC₅₀ of 1 x 10⁻¹¹ M or less.

148. (New) The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC₅₀ of 5 x 10⁻¹² M or less.

Claims 15-40. (Cancelled)

41. (Original) An isolated human antibody, or an antigen-binding portion thereof, which

- a) inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC₅₀ of 1 x 10⁻⁹M or less;
- b) has a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 25; and
- c) has a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 26.

149. **(New)** The isolated human antibody, or antigen-binding portion thereof, of claim 41, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC₅₀ of 1 x 10⁻¹⁰ M or less.

150. **(New)** The isolated human antibody, or antigen-binding portion thereof, of claim 41, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC₅₀ of 1 x 10⁻¹¹ M or less.

42. **(Original)** The isolated human antibody, or an antigen-binding portion thereof, of claim 41 which further has a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 27; and a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 28.

43. **(Original)** The isolated human antibody, or an antigen-binding portion thereof, of claim 41 which further has a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 29; and a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 30.

44. **(Original)** An isolated human antibody, or an antigen-binding portion thereof, having a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 31, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 32.

45. **(Original)** The isolated human antibody of claim 44, comprising a heavy chain constant region selected from the group consisting of IgG1, IgG2, IgG3, IgG4, IgM, IgA and IgE constant regions.
46. **(Original)** The isolated human antibody of claim 45, wherein the antibody heavy chain constant region is IgG1.
47. **(Original)** The isolated human antibody of claim 44, which is a Fab fragment.
48. **(Original)** The isolated human antibody of claim 44, which is a F(ab')₂ fragment.
49. **(Original)** The isolated human antibody of claim 44, which is a single chain Fv fragment.
- Claims 50-87. **(Canceled)**
88. **(Currently amended)** A pharmaceutical composition comprising the antibody or an antigen binding portion thereof, of claim 9 or 41, + and a pharmaceutically acceptable carrier.
89. **(Currently amended)** ~~A The pharmaceutical composition of claim 88, which further comprises comprising the antibody or an antigen binding position thereof, of claim 1 and an additional therapeutic agent.~~
90. **(Canceled)**
91. **(Currently amended)** The composition of claim 89 90, wherein the therapeutic agent is selected from the group consisting of budenoside, epidermal growth

factor, corticosteroids, cyclosporin, sulfasalazine, aminosalicylates, 6-mercaptopurine, azathioprine, metronidazole, lipoxygenase inhibitors, mesalamine, olsalazine, balsalazide, antioxidants, thromboxane inhibitors, IL-1 receptor antagonists, anti-IL-1 β monoclonal antibodies, anti-IL-6 monoclonal antibodies, growth factors, elastase inhibitors, pyridinyl-imidazole compounds, antibodies or agonists of TNF, LT, IL-1, IL-2, IL-6, IL-7, IL-8, IL-15, IL-16, IL-18, EMAP-II, GM-CSF, FGF, and PDGF, antibodies of CD2, CD3, CD4, CD8, CD25, CD28, CD30, CD40, CD45, CD69, CD90 or their ligands, methotrexate, cyclosporin, FK506, rapamycin, mycophenolate mofetil, leflunomide, NSAIDs, ibuprofen, corticosteroids, prednisolone, phosphodiesterase inhibitors, adenosine agonists, antithrombotic agents, complement inhibitors, adrenergic agents, IRAK, NIK, IKK, p38, MAP kinase inhibitors, IL-1 β converting enzyme inhibitors, TNF α converting enzyme inhibitors, T-cell signalling inhibitors, metalloproteinase inhibitors, sulfasalazine, azathioprine, 6-mercaptopurines, angiotensin converting enzyme inhibitors, soluble cytokine receptors, soluble p55 TNF receptor, soluble p75 TNF receptor, sIL-1RI, sIL-1RII, sIL-6R, antiinflammatory cytokines, IL-4, IL-10, IL-11, IL-13 and TGF β .

92. **(Currently amended)** The therapeutic composition of claim 89 90, wherein the therapeutic agent is selected from the group consisting of anti-TNF antibodies, and antibody fragments thereof, TNFR-Ig constructs, TACE inhibitors, PDE4 inhibitors, corticosteroids, budenoside, dexamethasone, sulfasalazine, 5-aminosalicylic acid, olsalazine, IL-1 β converting enzyme inhibitors, IL-1ra, tyrosine kinase inhibitors, 6-mercaptopurines and IL-11.

93-141 **(Canceled)**

151. **(New)** An isolated human antibody, or an antigen-binding portion thereof, which dissociates from human IL-12 with a K_d of 1 x 10⁻¹⁰ M or less and binds to an epitope on the p40 subunit of human IL-12.

152. **(New)** The isolated human antibody of claim 151, which neutralizes the activity of human IL-12.

153. (New) A neutralizing isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-3} \text{ s}^{-1}$ or less, as determined by surface plasmon resonance.

154. (New) The neutralizing isolated human antibody of claim 153, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-4} \text{ s}^{-1}$.

155. (New) The neutralizing isolated human antibody of claim 153, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-5} \text{ s}^{-1}$ or less.

156. (New) The neutralizing isolated human antibody of any one of claims 153 to 155, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of $1 \times 10^{-7} \text{ M}$ or less

157. (New) The neutralizing isolated human antibody of any one of claims 153 to 155, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of $1 \times 10^{-8} \text{ M}$ or less.

158. (New) The neutralizing isolated human antibody of any one of claims 153 to 155, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of $1 \times 10^{-9} \text{ M}$ or less.

159. (New) The neutralizing isolated human antibody of any one of claims 153 to 155, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of $1 \times 10^{-10} \text{ M}$ or less.

160. (New) The neutralizing isolated human antibody of any one of claims 153 to 155, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of $1 \times 10^{-11} \text{ M}$ or less.

161. (New) The neutralizing isolated human antibody of any one of claims 153 to 155, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC_{50} of $1 \times 10^{-10} \text{ M}$ or less.

162. (New) The neutralizing isolated human antibody of any one of claims 153 to 155, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC₅₀ of 1×10^{-11} M or less.

163. (New) The neutralizing isolated human antibody of any one of claims 153 to 155, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC₅₀ of 5×10^{-12} M or less.

164. (New) An isolated human antibody, or an antigen-binding portion thereof, which

- a) dissociates from human IL-12 with a k_{off} rate constant of 1×10^{-3} s⁻¹ or less, as determined by surface plasmon resonance;
- b) has a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 25; and
- c) has a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 26.

165. (New) The isolated human antibody of claim 164, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of 1×10^{-4} s⁻¹ or less.

166. (New) The isolated human antibody of claim 164, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of 1×10^{-5} s⁻¹ or less.

167. (New) An isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and comprises:

- a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 26; and
- a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 25.

168. (New) An isolated human antibody, or an antigen-binding portion thereof, with a light chain variable region (LCVR) having a CDR3 domain comprising the amino

acid sequence of SEQ ID NO: 26, and with a heavy chain variable region (HCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 25.

169. (New) The isolated human antibody, or an antigen-binding portion thereof, of claim 168, wherein the LCVR further has a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 28 and the HCVR further has a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 27.

170. (New) The isolated human antibody, or an antigen-binding portion thereof, of claim 169, wherein the LCVR further has CDR1 domain comprising the amino acid sequence of SEQ ID NO: 30 and the HCVR has a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 29.

171. (New) A pharmaceutical composition comprising an antibody or an antigen binding portion thereof, and a pharmaceutically acceptable carrier, wherein the antibody comprises:

a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 26; and

a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 25.

172. (New) An isolated human antibody that binds human IL-12 and is the antibody J695, or an antigen binding portion thereof.

173. (New) A pharmaceutical composition comprising the isolated human antibody of claim 172 and a pharmaceutically acceptable carrier.

174. (New) The pharmaceutical composition of claim 173, which further comprises at least one additional therapeutic agent.